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EXAMINER
WHITEMAN, BRIAN A

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1635	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/729,264	WELCHER ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *9,12-47,49-54 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11,48,55,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 1-8, 10, 11, 48, 55, and 57-58 are pending examination.

Applicants' traversal, amendment to claims 1-4, 11, 48, 55, cancellation claims 46 and 47, addition of claims 57-58 in paper no. are acknowledged and considered.

The objection to claims 1-8, 10-11, 46-48, and 55 are moot in view of the amendment to claims 1-3.

The objection to the specification is moot in view of the clarification by applicants.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10-11, 48, 55, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8, 10-11, 48, 55, 57 and 58, as best understood, is readable on a genus of a nucleotide sequence which hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence, wherein the nucleotide sequence has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6; a genus of a nucleotide sequence

encoding a polypeptide that is at least 70% identical to the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6, wherein the encoded polypeptide has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6; a genus of a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1, 3, or 5, or the claimed nucleotide sequences, wherein the encoded polypeptide has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6, wherein the genus of the claimed nucleic acid molecules is not claimed in a specific biochemical or molecule structure that could be envisioned by one skilled in the art at the time the invention was made.

The specification contemplates a genus of a nucleotide sequence which hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence, wherein the nucleotide sequence has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6; a genus of a nucleotide sequence encoding a polypeptide that is at least 70% identical to the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6, wherein the encoded polypeptide has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6; a genus of a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1, 3, or 5, or the claimed nucleotide sequences, wherein the encoded polypeptide has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6. The disclosure contemplates a nucleic acid sequence having B7-like activity. However, the specification does not provide sufficient description of a genus of polynucleotide sequences that possess any activity of SEQ ID NO: 2, 4, or 6. The state of the prior art displays that, "The B7 family of costimulatory molecules comprises B7.1 and B7.2 proteins, both of which can interact with two receptors, CD28 and CTLA-4, that are expressed by T cell proliferation, increasing

evidence indicates that they may not deliver identical signals to T cells, and that they may skew Th1 and Th2 phenotypes" (Li et al. Human Immunology, Vol. 61: 486-498, 2000). The specification does not provide sufficient description of what activity is possessed by the claimed nucleotide sequences that are considered B7-like activity. There are two different B7 proteins with different activities. It is not apparent that on the basis of the applicants' disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the claimed invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of nucleotide sequences that must exhibit the disclosed biological functions as contemplated by the specification.

The as-filed specification does not provide an adequate written description of a representative number of species of nucleotide sequences, which functions has an activity of SEQ ID NO: 2, 4, or 6. It is apparent from the state of the prior art exemplified by Ngo *et al.* (The Protein Folding Problem and Tertiary Structure Prediction, Birkhauser Boston, 1994, pp. 491-494) and Chiu *et al.* that the description of the primary sequence of amino acid residues in which the positions of the amino acid residues are particularly arranged is essential for the biological function of the protein encoded by the sequence. This essential element that is required for an adequate description of a representative number of species as embraced by the claimed genus of B-7 like encoded nucleic acid sequences is neither described sufficiently in the specification nor conventional in the prior art. A mere statement asserting that a nucleotide sequence which hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence, wherein the nucleotide sequence has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6; a nucleotide sequence encoding a polypeptide that is at

least 70% identical to the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6, wherein the encoded polypeptide has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6; a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1, 3, or 5, or the claimed nucleotide sequences, wherein the encoded polypeptide has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6 without providing the essential and specific arrangement of the amino acid residues positioned in the sequence does not lend evidentiary support for a skilled artisan to have recognized that applicant was in possession of the genus of B-7 like encoded nucleic acid sequences as claimed, particularly since the essential element of the coding sequence of a generic B-7 like nucleic acid molecule is lacking from the as-filed specification and since the skill and knowledge in the art is not adequate or conventional to determine the primary sequence of the representative number of species of B-7 like encoded genes or nucleic acids on the basis of the only disclosure of B-7 like polypeptides encoded in SEQ ID NO: 1, 3 or 5.

Vas-Cath Inc. v Mhurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purpose of the 'written description' inquiry, *whatever is now claimed.*" The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath, See MPEP 2163).

The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or the simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required.

See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v Chugai Pharmaceutical Co. Ltd., 18 USPQ 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification only provided the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997): *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement 'by describing the invention, with al it claimed limitations, not that which make it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc. that set forth the claimed invention." *Lockwood*, 107F.3d at 1572, 41 USPQ2d at 1966.

> An adequate written description of a DNA, such as the cDNA of the recombinant plasmid and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Dir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. At 1170, 25 USPQ at 1606.

> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information, concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is not further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes; as the example does, does not necessarily describe the cDNA itself. No sequence information indication which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, the claimed invention provides sufficient description of SEQ ID NO: 1, 3, or 5 or the nucleic acid sequence encoding SEQ ID NO: 2, 4 or 6, but not the activity that is considered B7 like activity or the full breadth of the claims (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

Applicants' traversal is not applicable to the new rejection under 112 written description.

Claims 1-8, 10, 11, 48, 55, 57, 58 as best understood, are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the presently pending claims encompassing any isolated polynucleotides or polypeptide sequence encoding a B-7 like molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient description (for possessing a genus of a nucleotide sequence which hybridizes under at least moderately stringent

conditions to the complement of the nucleotide sequence, wherein the nucleotide sequence has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6 as recited in the claims, particularly in view of the reasons set forth above, one skilled in the art would not have known how to make and use the claimed invention so that it would operate as intended; e.g. method of modulating levels of B7-like polypeptide in an animal.

The claimed invention is an isolated polynucleotide sequence (SEQ ID NOs 1, 3, or 5) encoding a B-7 like molecule and the amino acid sequences encoding a B-7 like molecule (SEQ ID NOs 2, 4, or 6). The specification defines a B-7 like nucleic acid sequence (e.g. gene, polypeptide, etc.) as comprising nucleotide sequence as set forth in 1, 3, or encoding SEQ ID NO: 2, 4, or 6 (pages 16-17). The as-filed specification encompasses determining the percent identity of the isolated nucleic acid molecule according to claim 2 using a computer program selected from GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm. The disclosure also claims nucleotide sequences, which hybridizes under moderate conditions to the complement of SEQ ID NOs 1-6 and a nucleotide sequence complementary to any nucleotide sequence encoding SEQ ID NOs: 1-6.

Furthermore, with respect to claims 1-3, the claimed invention is not considered enabled because the specification does not provide sufficient guidance for one skilled in the art to use any of the claimed sequences because the specification does not provide a function for the claimed sequences or how the sequences are similar in activity to a nucleic acid encoding a B7 protein. In view of the breadth of the term "B-7 like", the disclosure does not provide sufficient guidance (e.g. BLAST search, functional assay, etc.) or evidence for one skilled in the art to reasonably determine that any of these sequences have an activity of a nucleic acid encoding B7. In

addition, it is not apparent to one skilled in the art what biological properties consist of a B7-like molecule because the assertion that SEQ ID NO: 1-6 are most likely B-7 like nucleotides sequence does not provides sufficient guidance for one skilled in the art to use the nucleotide sequences and would result an undue amount of experimentation for one skilled in the art to use the nucleotide sequences. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the nucleotide sequence in many instances. The effects of these changes are largely unpredictable as to which mutation has a significant effect versus not. Therefore, the assertion of sequence similarity between the claimed sequences and B7 polypeptide without providing any guidance or evidence for the function of the claimed sequence results in an unpredictable and therefore unreliable correspondence between the claimed sequences and the indicated similar sequences of known function and therefore lacks support regarding enablement. Several publications document this unpredictability of the relationship between sequences and function, albeit that certain specific sequences may be found to be conserved over sequences of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Gerhold et al., (Bioassays, Vol. 18, page 973-981 (1996), Russell et al., (Journal of Molecular Biology, Vol. 244, pages 332-350 (1994), and Wells (Journal of Leukocyte Biology, Vol. 61, pages 545-550, 1997).

Furthermore, with respect to claims 1-3 and 11, in view of the state of the art and the as-filed specification, it is apparent that one skilled in the art would be able to determine the percent identity of a nucleotide sequence to any nucleotide sequence set forth in SEQ ID NOs: 1-6.

However, it not apparent to one skilled in the art how any of the claimed nucleic acid sequences correlate to a B-7 nucleic acid sequence or exhibits any biological activity (e.g. a biological activity of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6) as contemplated by the specification. The as-filed specification does not provide sufficient guidance or evidence for what nucleotides or amino acids are considered essential for B-7 like activity. Since, the relationship between a sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Chiu et al., *Folding and Design*, 1998, pp. 23-228), it would require an undue experimentation for one skilled in the art to arrive at peptides that have B7-like activity. In addition, in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 U.S.C. 112, first paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for the determination of other genetic sequences that are embraced by the claim. This is the case here. In other words, since it would require undue experimentation to identify peptides that have B7-like activity, it certainty would require undue experimentation to make their corresponding DNA and, therefore claims 1-3 and 11 are not enabled.

In addition, the claimed invention uses the nucleic acid molecule of claim 1, 2, or 3 in a method of modulating levels of a polypeptide in an animal (claim 55). With respect to claim 55, at the time the application was filed the state of the art for gene therapy as exemplified Anderson

et al., *Nature*, Vol. 392, pp. 25-30, April 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target

tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Therefore, at the time the application was filed gene therapy was considered unpredictable

The as-filed specification contemplates several methods of gene therapy using the polypeptides and polynucleotides of the claimed invention. As stated above, it is not apparent to one skilled in the art what biological properties consist of a B7-like molecule. The prior art recites that B-7, expressed on antigen presenting cells, provides a crucial co-stimulatory signal for T cell activation (Freeman et al., *J. Exp. Med.*, Vol. 178, 1993, pp. 2185-2191). The state of the prior art further displays that, "The B7 family of co-stimulatory molecules comprises B7.1 and B7.2 proteins, both of which can interact with two receptors, CD28 and CTLA-4, that are expressed by T cell proliferation, increasing evidence indicates that they may not deliver identical signals to T cells, and that they may skew Th1 and Th2 phenotypes" (Li et al). A sequence search of the prior art indicates that the closes related sequence is a novel human diagnostic protein (66.3 % identity, WO200175067, Drmanac et al.) with no similar function to a B7 protein. It is not apparent from the disclosure how the SEQ ID NOs: 1-6 are related to B-7 or what is a B7-like molecule. Furthermore, the as-filed specification does not provide sufficient guidance or evidence for how modulating levels of a B7-like polypeptide in an animal comprising administering to the animal the nucleic acid molecule of SEQ ID NOs: 1-6 correlates to a therapeutic effect in any animal. In addition, the breadth of the term "modulating" encompasses increasing or decreasing the level of the claimed nucleic acid molecule in an animal. One skilled in the art understands that a DNA sequence encoding a protein can be used

to increase expression of that particular protein in a system (e.g. animal, in vitro cell). However, the as-filed specification fails to provide sufficient guidance or evidence for how one skilled in the art would be enabled to use the claimed nucleic acids to decrease the levels of B-7 like gene products in an animal. One skilled in the art understands that nucleic acid encoding a protein cannot be used to decrease the level of a gene product in a system and that one skilled in the art would use a nucleic acid molecule selected from an anti-sense molecule, ribozyme, etc. for decreasing the level of expression of a gene product in a system. Thus, in view of In re Wands Factors, it would take one skilled in the art an undue amount of experimentation to determine how to use the nucleic acid sequences (SEQ ID NOs: 1, 3, or 5) and/or the nucleic acid sequences encoding the polypeptide sequences (SEQ ID NOs; 2, 4, or 6) any claimed method of modulating.

If the applicants are able to overcome the 112 enablement rejection for how to reasonably correlate the claimed sequences to a biological activity (e.g. co-stimulatory signal for T cell activation) of B7 protein or how to use the claimed sequences in the method of claim 55, there is another 112 enablement rejection for the phrase "any activity of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6".

With respect to claims encompassing a genus of a nucleotide sequence which hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence, wherein the nucleotide sequence has **an activity** of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6, the claims are not considered enabled because in view of the breadth of the phrase "moderately stringent conditions" and "any activity of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6". The specification defines "moderately stringent conditions" by providing an

example of this condition (see page 29) and does not define the lower and upper limit of the condition so that one skilled in the art can reasonably determine what sequences are not considered to hybridize to the claimed sequences. The claimed nucleotide sequences read on any sequence with one or more base pairs because of the term "complement". In addition, the breadth of the phrase "any activity of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6" encompasses any activity (e.g. antigenic) of the claimed sequence and any nucleotide sequence, including the claimed sequences could be considered to have antigenic activity when administered to an animal. The specification provides sufficient guidance for one skilled in the art to make a nucleotide sequence that hybridizes under moderately or highly stringent conditions to the full complement of the claimed nucleotide sequences, wherein the nucleotide sequence has B7 activity. However, for the reasons set forth above, the claims read on sequences that would not possess B7 activity. Thus, the as-filed specification does not provide sufficient guidance and evidence for one skilled in the art to make a nucleotide which hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence, wherein the nucleotide sequence has an activity of the polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made do not enable one skilled in the art to use the claimed invention. Given that gene therapy wherein any carrier is employed to correct a disease or a medical condition in any animal was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to how the biological function of any of the DNA molecules encoding a sequence (SEQ ID NOs 1-6) cited in the claims corresponds to a therapeutic effect in any animal,

one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of gene therapy.

Applicants traverse the rejection under 112 enablement for the following reasons: Applicants have amended claim 55 to indicate that the polypeptide to be modulated is a B-7 like polypeptide. The term for B-7 like polypeptide is defined in the specification on pages 16-17. Applicants have deleted claim 2(g) to render the rejection moot for nucleic acid molecules having a substitution or deletion of 1 to 100 amino acid residues in the claimed polypeptides. It would be apparent how to one skilled in the art how the nucleotides of claims 1(e), 2(k), and 3(l) would exhibit B-7 like polypeptide activity. See pages 6-7.

Applicants' traversal is acknowledged and is not found persuasive for the reasons set forth under the 112 enablement rejection.

The rejection under 112 second paragraph for the phrase "moderately stringent conditions" in claims 1-3 is moot because the term is broad and not indefinite.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 2, 3, 8, 10, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "B7-like polypeptide" in claims 8, 10, and 55 is a relative term, which renders the claim indefinite. The term "B7-like polypeptide" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of a B7-like polypeptide are not defined by the specification. One skilled in the art would look to the specification for the definition of a "B-7 like polypeptide" and the specification does not define the term. The specification defines that term as a SEQ ID NO: with no function or biological activity. Thus, the disclosure does not particularly point out and distinctly claim what is a "B-7 like polypeptide".

Applicants traverse the rejection because the specification defines the definition of B-7 like polypeptide at page 16, line 23-page 17, line 3 in the specification and contend that that this definition controls the interpretation of the phrase as it is used in the claims of the instant application. See page 8.

Applicants' traversal is acknowledged and is not found persuasive because the definition of the term is the term itself. The disclosure does not particularly point out and distinctly claim what is a "B-7 like polypeptide".

Claims 1-3 recite the limitation "the polypeptide as set forth in SEQ ID NO: 2, 4 or 6". There is insufficient antecedent basis for this limitation in the claim. Suggest amending the phrase to read as follows: a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NO: 2, 4, or 6.

Applicants' traversal is not applicable to the new rejections under 112 second paragraph.

Claims 1-3 recite the limitation "the encoded polypeptide". There is insufficient antecedent basis for this limitation in the claim.

Applicants' traversal is not applicable to the new rejections under 112 second paragraph.

The statement in claims 48 and 57, "... **a** nucleic acid molecule of any of claims 1, 2, or 3" is indefinite because it does not point out which molecule **a** nucleic acid molecule is referring to in the claim. The dependent claims should state ".... **the** nucleic acid molecule of any of claims 1, 2, or 3".

Applicants' traversal is not applicable to the new rejections under 112 second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 remain rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al. (The Washington University-NCI Mouse EST project, seq_name: gb_est82: BF040046, July 2, 1999). Marra discloses an EST sequence with 85% similarity to the claimed sequences, which is complementary to the nucleotide sequence from SEQ ID NO: 1-6.

Applicants traverse the 102 rejection because the nucleotide sequence of Marra and the claimed nucleotide sequences share no more than 72.6% identity over no more than 286 bp, a

nucleic acid molecule comprising the nucleotide sequence of Marra would not hybridize under moderately stringent conditions to the claimed nucleotides sequences. See page 9.

Applicants' traversal is acknowledged and to the extent that is applicable to the rejection under 102 it is not found persuasive. The sequence taught by Marra reads on the claimed sequence that is complementary to any of the claimed sequences. A sequence that is complementary would encompass a nucleotide with one base pair or more in common with any claimed sequence. Furthermore, Marra anticipates the claims because the breadth of the phrases "moderately stringent condition" and "an activity of the polypeptide as set forth in any SEQ ID NO: 2, 4, or 6". The breadth of the phrases encompasses any activity (e.g. antigenic) and the sequence taught by Marra is antigenic when administered to an animal. Thus, Marra anticipates the claimed sequences.

To overcome the prior art anticipating the complement sequences, suggest amending the phrase "a nucleotide sequence complementary to the nucleotide of any of (a)-(e)" to read as follows: nucleic acid sequence that is the full complement of the nucleotide of any of (a)-(e).

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Taudien et al. (NCBI [online] Bethesda, MD USA: United States National Library of Medicine [retrieved on 23 December 2002]. Retrieved from: NCBI, Accession Number AF121782). Taudien discloses a sequence that is complementary to the nucleotide sequences from SEQ ID NO: 1-6.

To overcome the prior art anticipating the complement sequences, suggest amending the phrase "a nucleotide sequence complementary to the nucleotide of any of (a)-(e)" in the claims to

read as follows: nucleic acid sequence that is the full complement of the nucleotide of any of (a)-(e).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
12/26/02

DAVE T. NGUYEN
PRIMARY EXAMINER